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=> s Wyatt, J?/au
L4        2533 WYATT, J?/AU

=> s l4 and antisense
L5          69 L4 AND ANTISENSE

=> s l5 and py<=2000
   1 FILES SEARCHED...
   3 FILES SEARCHED...
L6          22 L5 AND PY<=2000

=> dup l6 remove
PROCESSING COMPLETED FOR L6
L7           11 DUP REMOVE L6 (11 DUPLICATES REMOVED)

=> d l7 1-11 abs bib

L7   ANSWER 1 OF 11  CA  COPYRIGHT 2002 ACS
AB   The present invention provides compns. and methods for controlling the
     behavior of a cell, tissue or organism through antisense
     modulation of mRNA processing, using antisense compds. which do
     not support cleavage of the mRNA target.  Antisense
     oligonucleotides with 2'-methoxyethoxy (2'-MOE), 2'-dimethylaminooxyethoxy
     (2'-DMAOE), 2'-dimethylaminoethoxyethoxy, 2'-acetamide, morpholino or
     peptide nucleic acid modifications were synthesized with phosphodiester or
     phosphorothioate backbone linkages.  The modifications of
     antisense oligonucleotides were either uniform or gapped.  Effects
     of modified antisense oligonucleotides on mRNAs were detd. for
     interleukin 5 (IL-5) receptor .alpha. and Bcl-x.  Uniformly 2'-MOE
     oligonucleotides targeted to certain exons or intron/exon boundaries of
     the sol./membrane IL-5 receptor .alpha. caused reduced expression of the
     membrane form and increased expression of the sol. form.  Reduced cell
     surface expression of IL-5 receptor .alpha. protein, induction of
     apoptosis, and inhibition of cell proliferation in response to IL-5 by the
     2'-MOE antisense oligonucleotides were also measured.  The
     Bcl-xl (long) isoform of Bcl-x inhibits apoptosis while the Bcl-xs (short)
     isoform antagonizes Bcl-xl.  Uniformly 2'-MOE, phosphorothioate
     oligonucleotides (e.g. ISIS 22783) targeted to a region upstream of the 5'
     splice site of bcl-xl were found to increase the ratio of bcl-xs to
     bcl-xl.  After antisense treatment with the highly active ISIS
     22783, increased apoptosis of cells in response to UV stress,
     cisplatinum-induced cell death and taxol-induced cell death were
     quantitated.  An ISIS 22783 analog with 2'-DMAOE had a similar effect on
     the bcl-xs/bcl-xl mRNA ratio.
AN   134:275750  CA
TI   Alteration of cellular proliferation or apoptosis by antisense
     modulation of mRNA splicing, polyadenylation, or degradation
IN   Bennett, C. Frank; Cooke, Stanley T.; Manoharan, Muthiah; Wyatt,
     Jacqueline R.; Baker, Brenda F.; Monia, Brett P.; Freier, Susan M.;
     McKay, Robert; Karras, James G.
PA   Isis Pharmaceuticals, Inc., USA
SO   U.S., 39 pp., Cont.-in-part of U.S. Ser. No. 167,921.
     CODEN: USXXAM
DT   Patent
LA   English
FAN.CNT 4
     PATENT NO.          KIND  DATE          APPLICATION NO.  DATE
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PI   US 6210892          B1    20010403      US 1999-277020   19990326
     US 6172216          B1    20010109      US 1998-167921   19981007
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US 6214986 B1 20010410 US 1999-323743 19990602
WO 2000020432 A1 20000413 WO 1999-US22448 19990928 <--
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
AU 9962710 A1 20000426 AU 1999-62710 19990928 <--
EP 1119579 A1 20010801 EP 1999-949943 19990928
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO
US 2001007025 A1 20010705 US 2000-734846 20001212
PRAI US 1998-167921 A2 19981007
US 1999-277020 A2 19990326
US 1999-323743 A 19990602
WO 1999-US22448 W 19990928
RE.CNT 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 2 OF 11 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE 1

AB **Antisense** compounds, compositions and methods are provided for modulating the expression of E2F transcription factor 3. The compositions comprise **antisense** compounds, particularly **antisense** oligonucleotides, targeted to nucleic acids encoding E2F transcription factor 3. Methods of using these compounds for modulation of E2F transcription factor 3 expression and for treatment of diseases associated with expression of E2F transcription factor 3 are provided.

AN 2001:292608 BIOSIS
DN PREV200100292608
TI **Antisense** inhibition of E2F transcription factor 3 expression.
AU Popoff, Ian (1); **Wyatt, Jacqueline**
CS (1) Encinitas, CA USA
ASSIGNEE: Isis Pharmaceuticals, Inc.
PI US 6165791 December 26, 2000
SO Official Gazette of the United States Patent and Trademark Office Patents, (**Dec. 26, 2000**) Vol. 1241, No. 4, pp. No Pagination. e-file.
ISSN: 0098-1133.
DT Patent
LA English

L7 ANSWER 3 OF 11 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE 2

AB **Antisense** compounds, compositions and methods are provided for modulating the expression of methionine aminopeptidase 2. The compositions comprise **antisense** compounds, particularly **antisense** oligonucleotides, targeted to nucleic acids encoding methionine aminopeptidase 2. Methods of using these compounds for modulation of methionine aminopeptidase 2 expression and for treatment of diseases associated with expression of methionine aminopeptidase 2 are provided.

AN 2001:244666 BIOSIS
DN PREV200100244666
TI **Antisense** inhibition of methionine aminopeptidase 2 expression.
AU Monia, Brett P.; **Wyatt, Jacqueline (1)**
CS (1) Encinitas, CA USA
ASSIGNEE: Isis Pharmaceuticals Inc.
PI US 6136604 October 24, 2000
SO Official Gazette of the United States Patent and Trademark Office Patents,

(**Oct. 24, 2000**) Vol. 1239, No. 4, pp. No Pagination. e-file.
ISSN: 0098-1133.
DT Patent
LA English

L7 ANSWER 4 OF 11 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE 3
AB Design of **antisense** oligonucleotides targeting any mRNA can be much more efficient when several activity-enhancing motifs are included and activity-decreasing motifs are avoided. This conclusion was made after statistical analysis of data collected from >1000 experiments with phosphorothioate-modified oligonucleotides. Highly significant positive correlation between the presence of motifs CCAC, TCCC, ACTC, GCCA and CTCT in the oligonucleotide and its **antisense** efficiency was demonstrated. In addition, negative correlation was revealed for the motifs GGGG, ACTG, AAA and TAA. It was found that the likelihood of activity of an oligonucleotide against a desired mRNA target is sequence motif content dependent.
AN 2000:403310 BIOSIS
DN PREV200000403310
TI Identification of sequence motifs in oligonucleotides whose presence is correlated with **antisense** activity.
AU Matveeva, O. V. (1); Tsodikov, A. D.; Giddings, M.; Freier, S. M.; **Wyatt, J. R.**; Spiridonov, A. N.; Shabalina, S. A.; Gesteland, R. F.; Atkins, J. F.
CS (1) Department of Human Genetics, University of Utah, 15N 2030E Room 7410, Salt Lake City, UT, 84112-5330 USA
SO Nucleic Acids Research, (**August 1, 2000**) Vol. 28, No. 15, pp. 2862-2865. print.
ISSN: 0305-1048.
DT Article
LA English
SL English

L7 ANSWER 5 OF 11 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE 4
AB The secondary and tertiary structures of a mRNA are known to effect hybridization efficiency and potency of **antisense** oligonucleotides in vitro. Additional factors including oligonucleotide stability and cellular uptake are also thought to contribute to **antisense** potency in vivo. Each of these factors can be affected by the sequence of the oligonucleotide. Although mRNA structure is presumed to be a critical determinant of **antisense** activity in cells, to date little direct experimental evidence has addressed the significance of structure. In order to determine the importance of mRNA structure on **antisense** activity, oligonucleotide target sites were cloned into a luciferase reporter gene along with adjoining sequence to form known structures. This allowed us to study the effect of target secondary structure on oligonucleotide binding in the cellular environment without changing the sequence of the oligonucleotide. Our results show that structure does play a significant role in determining oligonucleotide efficacy in vivo. We also show that potency of oligonucleotides can be improved by altering chemistry to increase affinity for the mRNA target even in a region that is highly structured.
AN 2000:196376 BIOSIS
DN PREV200000196376
TI Effects of RNA secondary structure on cellular **antisense** activity.
AU Vickers, Timothy A. (1); **Wyatt, Jacqueline R.**; Freier, Susan M.
CS (1) Department of Molecular and Structural Biology, Isis Pharmaceuticals, 2280 Faraday Avenue, Carlsbad, CA, 92008 USA
SO Nucleic Acids Research, (**March 15, 2000**) Vol. 28, No. 6, pp.

1340-1347.
ISSN: 0305-1048.
DT Article
LA English
SL English

L7 ANSWER 6 OF 11 CA COPYRIGHT 2002 ACS
AB Iterative, preferably computer-based iterative, processes for generating synthetic compds. with desired phys., chem., and/or bioactive properties are provided. During iterations of the processes, a target nucleic acid sequence is provided or selected, and a library of candidate oligonucleotide sequences is generated in silico according to defined criteria. A "virtual" oligonucleotide chem. is chosen and a library of virtual oligonucleotides having the selected sequences is generated. These virtual compds. are reviewed and compds. predicted to have particular properties are selected. The selected compds. are robotically synthesized and are preferably robotically assayed for a desired phys., chem., or biol. activity. Active compds. are thus generated and, at the same time, preferred sequences and regions of the target nucleic acid that are amenable to oligonucleotide or sequence-based modulation are identified. The method was employed to identify phosphorothioate oligonucleotides targeted to CD40, RhoC, API-2, ELK-1, G.alpha.11, and AKT-1.
AN 131:307654 CA
TI Identification of genetic targets for oligonucleotides and generation of oligonucleotides for gene modulation
IN Cowsert, Lex M.; Baker, Brenda F.; Mcneil, John; Freier, Susan M.; Sasmor, Henri M.; Brooks, Douglas G.; Ohasi, Cara; **Wyatt, Jacqueline R.**; Borchers, Alexander H.; Vickers, Timothy A.
PA Isis Pharmaceuticals, Inc., USA
SO PCT Int. Appl., 264 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	WO 9953101	A1	19991021	WO 1999-US8268	19990413	<--
	W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG					
	US 2002028923	A1	20020307	US 1998-67638	19980428	
	CA 2325013	AA	19991021	CA 1999-2325013	19990413	<--
	AU 9939650	A1	19991101	AU 1999-39650	19990413	<--
	EP 1071826	A1	20010131	EP 1999-922713	19990413	
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI					
	JP 2002511276	T2	20020416	JP 2000-543647	19990413	
PRAI	US 1998-81483P	P	19980413			
	US 1998-67638	A2	19980428			
	WO 1999-US8268	W	19990413			

RE.CNT 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 7 OF 11 SCISEARCH COPYRIGHT 2002 ISI (R)
AB A computer program, OligoWalk, is reported that predicts the

equilibrium affinity of complementary DNA or RNA oligonucleotides to an RNA target. This program considers the predicted stability of the oligonucleotide-target helix and the competition with predicted secondary structure of both the target and the oligonucleotide, Both unimolecular and bimolecular oligonucleotide self structure are considered with a user-defined concentration. The application of OligoWalk is illustrated with three comparisons to experimental results drawn from the literature.

AN 1999:891635 SCISEARCH
GA The Genuine Article (R) Number: 255MD
TI Predicting oligonucleotide affinity to nucleic acid targets
AU Mathews D H; Burkard M E; Freier S M; **Wyatt J R**; Turner D H (Reprint)
CS UNIV ROCHESTER, DEPT CHEM, ROCHESTER, NY 14627 (Reprint); UNIV ROCHESTER, DEPT CHEM, ROCHESTER, NY 14627; ISIS PHARMACEUT, DIV MOL & STRUCT BIOL, CARLSBAD, CA 92008
CYA USA
SO RNA-A PUBLICATION OF THE RNA SOCIETY, (**NOV 1999**) Vol. 5, No. 11, pp. 1458-1469.
Publisher: CAMBRIDGE UNIV PRESS, 40 WEST 20TH STREET, NEW YORK, NY 10011-4211.
ISSN: 1355-8382.
DT Article; Journal
FS LIFE
LA English
REC Reference Count: 52
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

L7 ANSWER 8 OF 11 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE 5
AB Resistance to apoptosis, which plays an important role in tumors that are refractory to chemotherapy, is regulated by the ratio of antiapoptotic to proapoptotic proteins. By manipulating levels of these proteins, cells can become sensitized to undergo apoptosis in response to chemotherapeutic agents. Alternative splicing of the bcl-x gene gives rise to two proteins with antagonistic functions: Bcl-xL, a well-characterized antiapoptotic protein, and Bcl-xS, a proapoptotic protein. We show here that altering the ratio of Bcl-xL to Bcl-xS in the cell using an **antisense** oligonucleotide permitted cells to be sensitized to undergo apoptosis in response to ultraviolet B radiation and chemotherapeutic drug treatment. These results demonstrate the ability of a chemically modified oligonucleotide to alter splice site selection in an endogenous gene and illustrate a powerful tool to regulate cell survival.
AN 2000:42175 BIOSIS
DN PREV200000042175
TI Induction of endogenous Bcl-xS through the control of Bcl-x pre-mRNA splicing by **antisense** oligonucleotides.
AU Taylor, Jennifer K.; Zhang, Qing Qing; **Wyatt, Jacqueline R.**; Dean, Nicholas M. (1)
CS (1) Department of Pharmacology, Isis Pharmaceuticals, Carlsbad, CA USA
SO Nature Biotechnology, (**Nov., 1999**) Vol. 17, No. 11, pp. 1097-1100.
ISSN: 1087-0156.
DT Article
LA English
SL English

L7 ANSWER 9 OF 11 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1999:184663 BIOSIS
DN PREV199900184663
TI Upregulation of Bcl-xs through modulation of Bcl-x splicing by chemically modified **antisense** oligonucleotides.
AU Taylor, J. K.; Zhang, Q. Q.; Burkin, T.; Cooper, S.; **Wyatt, J.**;

Freier, S.; Dean, N. M.
CS Isis Pharm., Carlsbad, CA 92075 USA
SO Proceedings of the American Association for Cancer Research Annual Meeting, (**March, 1999**) Vol. 40, pp. 217-218.
Meeting Info.: 90th Annual Meeting of the American Association for Cancer Research Philadelphia, Pennsylvania, USA April 10-14, 1999 American Association for Cancer Research
. ISSN: 0197-016X.
DT Conference
LA English

L7 ANSWER 10 OF 11 CA COPYRIGHT 2002 ACS
AB Compns. and methods are provided for the treatment and diagnosis of herpesvirus infections. In accordance with preferred embodiments, oligonucleotides are provided which are specifically hybridizable with RNA or DNA deriving from a herpesvirus gene corresponding to one of the open reading frames UL5, UL8, UL9, UL20, UL27, UL29, UL30, UL42, UL52 and IE175 of herpes simplex virus type 1. The oligonucleotide comprises nucleotide units sufficient in identity and no. to effect said specific hybridization. In other preferred embodiments, the oligonucleotides are specifically hybridizable with a translation initiation site, a coding region or a 5'-untranslated region. Methods of treating animals suspected of being infected with herpesvirus comprising contacting the animal with an oligonucleotide of the invention are disclosed. Methods for treatment of infections caused by herpes simplex virus type 1, herpes simplex virus type 2, cytomegalovirus, human herpes virus 6, Epstein Barr virus or varicella zoster virus are disclosed.
AN 125:49274 CA
TI Oligonucleotide therapies for modulating the effects of herpes viruses
IN Draper, Kenneth G.; Crooke, Stanley T.; Mirabelli, Christopher K.; Ecker, David J.; Hanecak, Ronnie C.; Anderson, Kevin P.; Brown-Driver, Vickie L.; **Wyatt, Jacqueline R.**
PA Isis Pharmaceuticals, Inc., USA
SO U.S., 28 pp. Cont.-in-part of U.S. 5, 248, 670.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 6

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5514577	A	19960507	US 1993-31147	19930312 <--
	US 5248670	A	19930928	US 1990-485297	19900226 <--
	US 6310044	B1	20011030	US 1992-852132	19920428
	EP 1016715	A1	20000705	EP 1999-203835	19930929 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE				
	WO 9419945	A1	19940915	WO 1994-US2471	19940307 <--
	W: AU, BB, BG, BR, BY, CA, CN, CZ, FI, HU, JP, KP, KR, KZ, LK, LV, MG, MN, MW, NO, NZ, PL, RO, RU, SD, SK, UA, UZ, VN				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9463619	A1	19940926	AU 1994-63619	19940307 <--
	EP 692930	A1	19960124	EP 1994-910879	19940307 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
	JP 08503959	T2	19960430	JP 1994-520254	19940307 <--
	US 5658891	A	19970819	US 1994-329212	19941026 <--
PRAI	US 1990-485297	A2	19900226		
	US 1992-852132	A2	19920428		
	US 1992-954185	B2	19920929		
	WO 1991-US1327	W	19910225		
	US 1993-31147	A	19930312		
	US 1993-122328	B1	19930916		
	EP 1993-922788	A3	19930929		

WO 1994-US2471 W 19940307

L7 ANSWER 11 OF 11 SCISEARCH COPYRIGHT 2002 ISI (R)

AB Phosphorothioate oligonucleotides were identified which directly inhibited human type II phospholipase A(2) (PLA(2)) enzyme activity in a sequence specific manner. The minimum pharmacophore common to all oligonucleotides which inhibited FLAP enzyme activity consisted of two sets of three or more consecutive guanosine residues in a row. These oligonucleotides appear to form G quartets resulting in the formation of oligonucleotide aggregates. Additionally, a phosphorothioate backbone was required to be effective inhibitors of type II PLA(2). The activity of one oligodeoxynucleotide, IP 3196 (6'-GGGTGGGTATAGAAGGGCTCC-3') has been characterized in more detail. IP 3196 inhibited PLA(2) enzyme activity when the substrate was presented in the form of a phospholipid bilayer but not when presented in the form of a mixed micelle with anionic detergents. Human type II PLA, was 50-fold more sensitive to inhibition by IP 3196 than venom and pancreatic type I enzymes. These data demonstrate that phosphorothioate oligonucleotides can specifically inhibit human type II PLA(2) enzyme activity in a sequence specific manner.

AN 94:537131 SCISEARCH

GA The Genuine Article (R) Number: PD657

TI SEQUENCE-SPECIFIC INHIBITION OF HUMAN TYPE-II PHOSPHOLIPASE A(2) ENZYME-ACTIVITY BY PHOSPHOROTHIOATE OLIGONUCLEOTIDES

AU BENNETT C F (Reprint); CHIANG M Y; WILSONLINGARDO L; **WYATT J R**

CS ISIS PHARMACEUT, DEPT MOLEC PHARMACOL, 2292 FARADAY AVE, CARLSBAD, CA, 92008 (Reprint); ISIS PHARMACEUT, DEPT BIOL MOLEC & STRUCT, CARLSBAD, CA, 92008

CYA USA

SO NUCLEIC ACIDS RESEARCH, (**11 AUG 1994**) Vol. 22, No. 15, pp. 3202-3209.
ISSN: 0305-1048.

DT Article; Journal

FS LIFE

LA ENGLISH

REC Reference Count: 63
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

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